REMARKS

Applicants wish to thank Examiner Holleran for her time and comments during an interview with Dr. Jeremy Chrisp and Applicants' representative, Dr. William Christiansen, on August 10, 2004. Possible claim amendments and arguments for rebutting the obviousness rejections were discussed.

Reconsideration of the present application in view of the above amendments and the following remarks is respectfully requested. The election of a species requirement set forth in the Office Action mailed October 2, 2002 has been withdrawn. Accordingly, claims 1, 2, and 7-21 are pending and currently under examination. Applicants have amended claims 1 and 7-17 to define more clearly certain subject matter encompassed by Applicants' invention. Support for the amended claims can be found throughout the specification, for example, at page 26, lines 11-20; page 27, lines 11-18; page 32, lines 27-30; page 35, lines 9-18; page 35, line 20 through page 36, line 5; page 44, line 24 through page 45, line 9; page 47, lines 15-22. No new matter has been added.

REJECTION UNDER 35 U.S.C. § 112, FIRST PARAGRAPH (WRITTEN DESCRIPTION)

Claims 1, 2, and 7-21 stand rejected under 35 U.S.C. § 112, first paragraph, for allegedly being directed to subject matter that is not adequately described in the specification. Specifically, the Action asserts that the method of claim 1, which recites that immunoglobulin molecules are specific for at least "five CD antigens," has no support in the specification and introduces new matter.

Applicants respectfully traverse this rejection and submit that in view of the amendments to claim 1 submitted herewith, the basis for this rejection has been obviated. Claim 1 is directed in pertinent part to a method for identifying a type of leukemia in a human subject, which method comprises contacting cells in a biological sample with an array of immunoglobulin molecules that are specific for at least *seven* surface marker antigens. As described in the specification, immunoglobulin molecules

with distinct specificities are immobilized to different regions, or spots, on a matrix or solid support (*see, e.g.,* page 34, line 18 through page 35, line 18). Preferably the number of immunoglobulin regions is from 7 to 1000; accordingly, the immunoglobulins immobilized onto these regions bind to at least seven and as many as 1000 different antigens (*see, e.g.,* page 35, lines 9-18).

Applicants therefore respectfully submit that the claimed subject matter is sufficiently described in the specification to reasonably convey to a person skilled in the art that Applicants possessed the claimed invention at the time the Application was filed. Accordingly, Applicants submit that the instant Application complies with the written description requirement under 35 U.S.C. § 112, first paragraph, and respectfully request that the rejection be withdrawn.

REJECTIONS UNDER 35 U.S.C. § 103

Claims 1, 2, 7, 8, 11, 15, and 18-21 stand rejected under 35 U.S.C. § 103, allegedly for being obvious over Chang (U.S. Patent No. 4,591,570) in view of Valet (*Cytometry* 30:275-88 (1997)). The Action concedes that Chang fails to teach or suggest that antibodies specific for CD antigens may be used for identifying a type of leukemia. However, the Action alleges that Chang teaches a method for using antibodies immobilized to a solid support for differentiating different cell populations characterized by differential antigen expression. The Action asserts that Valet teaches a flow cytometric method in which antibodies specific for CD antigens may distinguish different types of leukemias. The Action further asserts that a person having ordinary skill in the art would have been motivated to obtain Applicants' invention by modifying the method of Chang with the teachings of Valet for identifying a type of leukemia.

Applicants respectfully traverse this ground of rejection and submit that the claims meet the requirements for nonobviousness. Applicants respectfully submit that the Action has not established a *prima facie* case of obviousness. *See In re Mayne*, 104 F.3d 1339, 1341-43, 41 U.S.P.Q.2d 1451 (Fed. Cir. 1997) (PTO has the burden of showing a *prima facie* case of obviousness.). The PTO must show (1) that the references

teach or suggest all claim limitations; (2) that the references provide some teaching, suggestion, or motivation to combine or modify the teachings of the prior art to produce the claimed invention; and (3) that the combined teachings of the references indicate that by combining the references, a person having ordinary skill in the art will achieve the claimed invention with a reasonable expectation of success. When rejection of claims depends upon a combination of prior art references, something in the prior art as a whole must suggest the desirability, thus the obviousness, of making the combination (*see In re Rouffet*, 149 F.3d 1350, 1355, 47 U.S.P.Q.2d 1453 (Fed. Cir. 1998)).

As discussed herein, and in the accompanying Declaration under 37 C.F.R. § 1.132 of Professor Richard Ian Christopherson, a *prima facie* case of obviousness has not been established. Chang and Valet, alone or in combination, fail to teach or suggest each and every limitation of the present claims. As conceded by the Action, Chang fails to teach or suggest a method for identifying a type of leukemia by contacting cells from a human subject with an array of immunoglobulin molecules that are specific for at least seven cell surface marker antigens. Furthermore, Chang fails to teach or suggest or provide any motivation to use the method described therein for identifying or monitoring *any* disease state.

Chang also fails to teach or suggest that binding of an array of immunoglobulins to different cell surface antigens results in a discriminatory image of antigen expression that is characteristic of a type of leukemia. The discriminatory image of antigen expression indicates the relative density of interaction between each immunoglobulin and its cognate cell surface antigen, which may result, for example, from differential density of cells that bind to a discrete spot on the array, the differential expression of particular antigens, and/or the number of antigens per cell (*see, e.g.,* specification, page 26, lines 11-20). The resulting identifiable signal therefore may not vary only with a particular cell type but with expression of a particular antigen on different cell types, which results in a pattern of interaction that may be visualized as an image and/or quantified *(see, e.g.,* specification, page 47, lines 15-22; Tables 1-8). Chang fails to teach or suggest establishing a discriminatory image of antigen expression

to identify cell types but instead describes using a uniform layer of bound cells to cover the entire antibody-coated spot to facilitate detection (*see* Chang, column 3, lines 9-30). Chang is silent regarding a discriminatory or differential pattern of density, which provides an identifiable signal.

Valet also fails to teach or suggest a method for identifying a type of leukemia by contacting cells from a human subject with an array of immunoglobulin molecules immobilized to a solid surface. Valet further fails to teach or suggest a method comprising contacting a cell in a biological sample with immunoglobulin molecules specific for at least seven cell surface markers, and determining which surface marker antigens bind to which immunoglobulins to establish a discriminatory image of antigen expression, which is a differential pattern of density providing an identifiable signal, and that is characteristic of a type of leukemia. Valet teaches a flow cytometry method that uses triple matrix classifiers, that is, groups of three antibodies specific for three different cellular antigens analyzed as a single parameter in three separate samples, to generate a triple matrix database. Thus, Valet fails to teach the claimed method that comprises concurrent analysis of the separate interaction between the immunoglobulins of the array and at least seven cell surface marker antigens.

Applicants further submit that Valet provides nothing more than a cumulative reference in view of those cited in the instant specification that describe cell surface antigens that are expressed by leukocytes (*see, e.g.,* specification, page 3-4). Valet teaches that the method disclosed therein is used for discriminating among CLL, lymphoplasmocytoid immunocytoma (LP-IC) and other non-Hodgkin' lymphomas; Valet does not teach that particular CD antigens are expressed on cells from patients with CLL, HCL, ALL, or AMoL as listed in the Action (*see* Action, page 5, second full paragraph). Applicants are unclear regarding the source of the information in the Action regarding its assertion of which CD antigens are expressed by the particular leukemia cells listed. Applicants submit that even if Valet taught which CD antigens are expressed on cells from patients with CLL and ALL, for example, that because the CD antigens listed in the Action are identical, a person having ordinary skill in the art would not find it obvious in

view of the alleged teaching in Valet to obtain Applicants' claimed method for identifying a type of leukemia on the basis of a discriminatory image of antigen expression, which is a differential pattern of density providing an identifiable signal, that is characteristic of a type of leukemia.

Applicants respectfully disagree with the assertion in the Action that a person having ordinary skill in the art would have been motivated to combine the teachings of Chang and Valet to achieve Applicants' invention (*see also* Christopherson Declaration). As discussed above, Chang merely teaches a general method for analyzing multiple antibody-antigen binding interactions and fails to provide any suggestion or motivation for using the method for identifying a type of leukemia in a human subject. A general incentive, such as Chang's suggestion that the Chang method could be used instead of a fluorescent flow cytometry method does not make obvious the claimed method for identifying types of leukemia cells comprising binding of antibodies to cell surface antigens expressed on cells to obtain a discriminatory image that is characteristic of a type of leukemia (*see In re Deuel*, 51 F.3d 1552, 1559 (Fed. Cir. 1995) (affirming that a general incentive does not make obvious a particular result). Valet also fails to provide any motivation or indicate any desirability for combining its teachings with any other prior art teachings to achieve Applicants' invention. Valet lacks any suggestion that modification of the procedures disclosed therein is desirable; Valet teaches that a triple matrix pattern, even a single triple matrix pattern (*i.e.*, three antibodies specific for three different antigens), meets the criteria set forth in Valet for classification of leukocytes (*see, e.g.*,. Valet, pages 286-287).

Accordingly, neither cited document teaches, suggests, or provides any motivation for a skilled artisan to modify the method of Chang with the teachings of Valet to achieve successfully Applicants' method for determining a type of leukemia that comprises an array of immunoglobulins that are specific for at least seven cell surface antigens, wherein interaction between the immunoglobulins and the cell surface antigens establishes a discriminatory image of antigen expression that is characteristic of a type of leukemia.

Applicants therefore respectfully submit that the claims meet the requirements for nonobviousness under 35 U.S.C. § 103 and request that the rejection be withdrawn.

Claims 1, 2, and 7-20 also stand rejected under 35 U.S.C. § 103, allegedly for being obvious over Chang (U.S. Patent No. 4,591,570) in view of Terstappen (U.S. Patent No. 5,234,816). As discussed above, the Action concedes that Chang fails to teach or suggest that antibodies specific for CD antigens may be used for identifying a type of leukemia. However, the Action alleges that Chang teaches a method for using antibodies immobilized to a solid support for differentiating different cell populations characterized by differential antigen expression. The Action asserts that Terstappen teaches a flow cytometric method in which antibodies specific for CD antigens may distinguish different types of leukemias. The Action further asserts that a person having ordinary skill in the art would have been motivated to modify the method of Chang with the teachings of Terstappen for identifying a type of leukemia to obtain Applicants' invention.

Applicants respectfully traverse this ground of rejection and submit that the claims meet the requirements for nonobviousness. Applicants respectfully submit that the Action has not established a *prima facie* case of obviousness. Neither cited document, alone or in combination, teaches or suggests each and every limitation of the pending claims. As noted above, and as conceded by the Action, Chang fails to teach or suggest a method for identifying a type of leukemia by contacting cells from a human subject with an array of immunoglobulin molecules that are specific for at least seven cell surface marker antigens. Furthermore, Chang fails to teach or suggest or provide any motivation to use the method described therein for identifying or monitoring *any* disease state.

In addition, and as discussed in detail above, Chang also fails to teach or suggest that binding of an array of immunoglobulins to different cell surface antigens establishes a discriminatory image of antigen expression (*e.g.*, a differential pattern of density providing an identifiable signal) that is characteristic of a type of leukemia.

Chang fails to teach or suggest establishing a discriminatory image of antigen expression to identify cell types but instead describes using a uniform layer of bound cells to cover the entire antibody-coated spot to facilitate detection (*see* Chang, column 3, lines 9-30). Chang is silent regarding a discriminatory or differential pattern of density, which is provided by an identifiable signal.

Terstappen also fails to teach or suggest a method for identifying a type of leukemia by contacting cells from a human subject with an array of immunoglobulin molecules immobilized to a solid surface and determining which surface marker antigens have bound to which immobilized immunoglobulin molecules to establish a discriminatory image of antigen expression that is characteristic of a type of leukemia . Terstappen fails to teach concurrent analysis of each immunoglobulin/antigen binding interaction and instead teaches a *sequential* analysis of *antibody pairings*. Terstappen further teaches that the sequence of cell aliquot analysis and antibody pairing is important for practicing the method disclosed therein (*see* Terstappen, column 2, lines 51-65). (*See also* Christopherson Declaration).

Furthermore, modifying the method disclosed in Chang according to the teachings of sequential analysis of antibody pairings in Terstappen would change the principle of operation of Chang, which is to analyze binding of multiple antibodies and antigens simultaneously. Thus, a person having ordinary skill in the art could not have found it obvious to combine the teachings of Chang and Terstappen to obtain Applicants' claimed method that comprises concurrently establishing individual antibody/cell surface antigen binding interactions to provide a discriminatory image that is characteristic of a type of leukemia (*see, e.g., In re Ratti,* 270 F.2d 810, 813 (CCPA 1959) (holding that a *prima facie* case for obviousness had not been established when the suggested combination of references would require a reconstruction and redesign of the elements shown in the primary reference as well as a change in the basic principle under which the primary reference was designed to operate); MPEP § 2143.01).

Applicants further submit that Terstappen provides nothing more than a cumulative reference in view of those cited in the instant specification that describe cell

surface antigens that are expressed by leukocytes (*see, e.g.,* specification, page 3-4). Applicants note that Terstappen does not teach that particular CD antigens are expressed on cells from patients with CLL, HCL, CML, AML, ALL, AMML, AEL, AmegL, AMoL, NHL, or APL as listed in the Action (*see* Action, page 6, third paragraph). Applicants are unclear regarding the source of the information in the Action regarding its assertion of which CD antigens are expressed by the listed types of leukemia cells. Applicants submit that even if Terstappen taught which CD antigens are expressed on cells from patients with CLL and ALL or from patients with AMML, AEL, AmegL, and APL, for example, that because the CD antigens listed in the Action for both CLL and ALL are identical, and the CD antigens listed in the Action for AMML, AEL, AmegL, and APL are identical, a person having ordinary skill in the art would not find it obvious in view of the alleged teaching in Terstappen to obtain Applicants' claimed method for identifying a type of leukemia on the basis of a discriminatory image (e.g., a differential pattern of density providing an identifiable signal) that is characteristic of a type of leukemia.

Also as discussed above, Chang fails to suggest, teach, or motivate a person having ordinary skill in the art to combine its teachings with any other prior art teaching to obtain Applicant's invention (*see also* Christopherson Declaration). As discussed above, Chang merely teaches a general method for analyzing multiple antibody-antigen binding interactions and fails to provide any suggestion or motivation for using the method for identifying a type of leukemia in a human subject. A general incentive, such as Chang's suggestion that the Chang method could be used instead of a fluorescent flow cytometry method does not make obvious the claimed method for identifying types of leukemia cells comprising binding of antibodies to cell surface antigens expressed on cells to obtain a discriminatory image that is characteristic of a type of leukemia (*see In re Deuel*, 51 F.3d 1552, 1559 (Fed. Cir. 1995) (affirming that a general incentive does not make obvious a particular result). Terstappen also fails to provide any teaching, suggestion, or motivation to combine or modify the teachings of the prior art to produce Applicants' claimed method. Terstappen teaches a method for

classifying leukemias that uses different techniques and analyses and does not remotely suggest any desirability to combine the teachings therein with any other prior art to achieve Applicants' invention. Thus, the Action has failed to establish a *prima facie* case of obviousness because the cited documents lack the requisite suggestion or motivation to combine the teachings therein to obtain Applicants' claimed method.

Applicants therefore respectfully submit that the claims meet the requirements for nonobviousness under 35 U.S.C. § 103 and request that this rejection be withdrawn.

The Action rejects claims 1, 2, 7, 9-15, and 17-20 under 35 U.S.C. § 103, asserting that the claimed subject matter is obvious over Chang (U.S. Patent No. 4,591,570) in view of Verwer (U.S. Patent No. 5,605,805). As discussed above, the Action concedes that Chang fails to teach or suggest that antibodies specific for CD antigens may be used for identifying a type of leukemia. However, the Action alleges that Chang teaches a method for using antibodies immobilized to a solid support for differentiating different cell populations characterized by differential antigen expression. The Action asserts that Verwer teaches a flow cytometric method in which antibodies specific for CD antigens may distinguish different types of leukemias. The Action further asserts that a person having ordinary skill in the art would have been motivated to modify the method of Chang with the teachings of Verwer related to identifying a type of leukemia to obtain Applicants' invention.

Applicants respectfully traverse this ground of rejection and submit that the Action has not established a *prima facie* case of obviousness and that the claims meet the requirements for nonobviousness. Neither cited document, alone or in combination, teaches or suggests each and every limitation of the pending claims. As noted above, and as conceded by the Action, Chang fails to teach or suggest a method for identifying a type of leukemia by contacting a biological sample comprising cells from a human subject with an array of immunoglobulin molecules that are specific for at least seven cell surface marker antigens. Furthermore, Chang fails to teach or suggest or provide any

motivation to use the method described therein for identifying or monitoring *any* disease state.

In addition, and as discussed in detail above, Chang also fails to teach or suggest that binding of an array of immunoglobulins to different cell surface antigens results in a discriminatory image of antigen expression, such as provided by an identifiable signal. Chang fails to teach or suggest establishing a discriminatory image of antigen expression to identify cell types but instead describes using a uniform layer of bound cells to cover the entire antibody-coated spot to facilitate detection (*see* Chang, column 3, lines 9-30). Chang is silent regarding a discriminatory or differential pattern of density.

Verwer also fails to teach or suggest a method for identifying a type of leukemia by contacting cells from a single sample with an array of immunoglobulin molecules immobilized to a solid surface, and which array comprises antibodies that are specific for at least seven different cell surface marker antigens, and determining which surface marker antigens have bound to which immobilized immunoglobulin molecules to establish a discriminatory image of antigen expression that is characteristic of a type of leukemia. Verwer fails to teach or suggest concurrent analysis of multiple individual antibody/antigen interactions and instead teaches multiple analyses of antibody/antigen pairings (*see* Verver throughout). Moreover, Verwer teaches a data analysis technique for specifically analyzing flow cytometry data, wherein the technique provides positional information of cell clusters that is matched across multiple aliquots of a sample (Verwer, column 3, lines 7-11). (*See also* Christopherson Declaration).

Applicants further submit that Verwer provides nothing more than a cumulative reference in view of those cited in the instant specification that describe cell surface antigens that are expressed by leukocytes (*see, e.g.,* specification, page 3-4). Applicants also note that Verwer does not teach that particular CD antigens are expressed on cells from patients with CLL, CML, AML, ALL, AMML, AEL, AmegL, AMoL, or APL as listed in the Action (*see* Action, page 7, third paragraph). Applicants are unclear regarding the source of the information in the Action relating to its assertion of which CD

antigens are expressed by the listed types of leukemia cells. Applicants submit that even if Verwer taught which CD antigens are expressed on cells from patients with CLL and ALL or from patients with AMML, AEL, AmegL, AMoL, and APL, for example, that because the CD antigens listed in the Action for CLL and ALL are identical, and the antigens listed for AMML, AEL, AmegL, AMoL, and APL are identical, a person having ordinary skill in the art would not find it obvious in view of the alleged teaching in Verwer to obtain Applicants' claimed method for identifying a type of leukemia on the basis of a discriminatory image of antigen expression that is characteristic of a type of leukemia.

Moreover, and as discussed above, Chang fails to suggest, teach, or motivate a person having ordinary skill in the art to combine its teachings with any other prior art teaching to obtain Applicant's invention (*see also* Christopherson Declaration). Chang merely teaches a general method for analyzing multiple antibody-antigen binding interactions and fails to provide any suggestion or motivation for using the method for identifying a type of leukemia in a human subject. A general incentive, such as Chang's suggestion that the Chang method could be used instead of a fluorescent flow cytometry method does not make obvious the claimed method for identifying types of leukemia cells comprising binding of antibodies to cell surface antigens expressed on cells to obtain a discriminatory image that is characteristic of a type of leukemia (*see In re Deuel*, 51 F.3d 1552, 1559 (Fed. Cir. 1995) (affirming that a general incentive does not make obvious a particular result). Verwer also fails to provide any teaching, suggestion, or motivation to combine or modify the teachings of the prior art to produce Applicants' claimed method (*see also* Christopherson Declaration). Verwer teaches a method for classifying leukemias that uses different techniques and analyses and does not suggest any desirability to combine the teachings therein with any other prior art to achieve Applicants' method for identifying a type of leukemia in a human. Thus, the Action has failed to establish a *prima facie* case of obviousness because the cited documents lack the requisite suggestion or motivation to combine the teachings therein to obtain Applicants' claimed method.

Applicants therefore respectfully submit that the claims meet the requirements for nonobviousness under 35 U.S.C. § 103 and request that this rejection be withdrawn.

Claims 1, 2, 7, and 18-20 stand rejected under 35 U.S.C. § 103, allegedly for being obvious over Chang (U.S. Patent No. 4,591,570) in view of Orfao de Matos Correira E Vale (U.S. Patent No. 5,538,855). As discussed above, the Action concedes that Chang fails to teach or suggest that antibodies specific for CD antigens may be used for identifying a type of leukemia. However, the Action alleges that Chang teaches a method for using antibodies immobilized to a solid support for differentiating different cell populations characterized by differential antigen expression. The Action asserts that Orfao de Matos Correira E Vale teaches that a series of antibodies that are specific for CD antigens may be used to distinguish different subsets of lymphoid populations. The Action further asserts that different leukemias arise from different subsets of lymphoid populations and that the purpose of methods taught in Orfao de Matos Correira E Vale is the same as the purpose of Applicants' claimed methods. The Action alleges that a person having ordinary skill in the art would have been motivated to modify the method of Chang with the teachings of Orfao de Matos Correira E Vale to obtain Applicants' invention.

Applicants respectfully traverse this ground of rejection and submit that the Action has not established a *prima facie* case of obviousness and that the present claims meet the requirements for nonobviousness. Neither cited document, alone or in combination, teaches or suggests each and every limitation of the pending claims. As noted above, and as conceded by the Action, Chang fails to teach or suggest a method for identifying a type of leukemia by contacting cells from a human subject with an array of immunoglobulin molecules that are specific for at least seven cell surface marker antigens. Furthermore, Chang fails to teach or suggest or provide any motivation to use the method described therein for identifying or monitoring *any* disease state.

In addition, and as discussed in detail above, Chang also fails to teach or suggest that binding of an array of immunoglobulins to different cell surface antigens results in a discriminatory image of antigen expression, such as provided by an identifiable signal. Chang fails to teach or suggest establishing a discriminatory image of antigen expression to identify cell types but instead describes using a uniform layer of bound cells to cover the entire antibody-coated spot to facilitate detection (*see* Chang, column 3, lines 9-30). Chang is silent regarding a discriminatory or differential pattern of density.

Orfao de Matos Correira E Vale also fails to teach or suggest a method for identifying a type of leukemia; fails to teach or suggest that such a method comprises contacting cells from a human subject with an array of immunoglobulin molecules that are immobilized to a solid surface; fails to teach or suggest that the immunoglobulin molecules are specific for and capable of detecting concurrently at least seven cell surface marker antigens; and fails to teach or suggest determining which surface marker antigens have bound to which immobilized immunoglobulin molecules to establish a discriminatory image of antigen expression that is characteristic of a type of leukemia. Orfao de Matos Correira E Vale teaches a flow cytometry method for distinguishing T, B, and NK cells and subsets of same on the basis of which CD antigens are expressed. Expression of CD antigens as taught in Orfao de Matos Correira E Vale, such as CD3, CD4, and CD8, on lymphocytes and detection of these antigens with antibodies has been long known in the immunology art. Orfao de Matos Correira E Vale fails to teach or, in any manner, suggest that the CD antigen/antibody interactions disclosed therein may be applicable to any method for identifying a type of leukemia in a human subject. (*See also* Christopherson Declaration).

Moreover, and as discussed above, Chang fails to suggest, teach, or motivate a person having ordinary skill in the art to combine its teachings with any other prior art teaching to obtain Applicant's invention. Also as discussed above, Chang merely teaches a general method for analyzing multiple antibody-antigen binding interactions and fails to provide any suggestion or motivation for using the method for

identifying a type of leukemia in a human subject. A general incentive, such as Chang's suggestion that the Chang method could be used instead of a fluorescent flow cytometry method does not make obvious the claimed method for identifying types of leukemia cells comprising binding of antibodies to cell surface antigens expressed on cells to obtain a discriminatory image that is characteristic of a type of leukemia (*see In re Deuel*, 51 F.3d 1552, 1559 (Fed. Cir. 1995) (affirming that a general incentive does not make obvious a particular result). Orfao de Matos Correira E Vale also fails to provide any teaching, suggestion, or motivation to combine or modify the teachings of the prior art to produce Applicants' claimed method (*see also* Christopherson Declaration). Orfao de Matos Correira E Vale teaches a method for identifying subsets of lymphocytes using a different technique and analysis and does not suggest any desirability whatsoever to combine the teachings therein with any other prior art to achieve Applicants' method for identifying a type of leukemia in a human. Thus, the Action has failed to establish a *prima facie* case of obviousness because the cited documents lack the requisite suggestion or motivation to combine the teachings therein to obtain Applicants' claimed method.

Applicants therefore respectfully submit that the claims meet the requirements for nonobviousness under 35 U.S.C. § 103 and request that this rejection be withdrawn.

Claims 1, 2, 7-19, and 21 stand rejected under 35 U.S.C. § 103, allegedly for being obvious over Hoeffler (U.S. Publication No. 2002/0164656) in view of Terstappen (U.S. Patent No. 5,234,816). The Action concedes that Hoeffler fails to teach or suggest using arrays comprising antibodies that specifically bind to CD antigens. The Action asserts, however, that Hoeffler teaches a method of using microarrays comprising antibodies for cell profiling. The Action asserts that Terstappen teaches that antibodies specific for CD antigens may be used for distinguishing different types of leukemia. The Action further asserts that a person having ordinary skill in the art would have found it

obvious at the time the instant application was filed to obtain Applicants' invention by modifying the method of Hoeffler in view of the teachings of Terstappen.

Applicants respectfully traverse this ground of rejection and submit that the Action has not established a *prima facie* case of obviousness and that the claims meet the requirements for nonobviousness. Neither cited document, alone or in combination, teaches or suggests each and every limitation of the pending claims. As conceded by the Action, Hoeffler fails to teach a method that comprises immunoglobulins that are specific for CD antigens, which are cell surface antigens. Heoffler also fails to teach or suggest contacting cells in a biological sample with an array of immunoglobulin molecules, wherein the cells express a cell surface antigen present on a leukocyte. Hoeffler is silent with regard to using intact cells in the methods taught therein. Hoeffler teaches that antigens used in the method described therein are often proteins, although the antigens may be organic chemical compounds, carbohydrates, nucleic acids, and that the antigens may be isolated or semi-isolated, whether recombinantly made or naturally occurring (Hoeffler, paragraph 42). For example, the cited document teaches that activated T-cells may be distinguished from resting T-cells by contacting cell lysates with the array. Hoeffler further fails to teach or suggest a method for identifying a type of leukemia in a human subject comprising immunoglobulins that are specific for at least seven cell surface antigens and determining which surface marker antigens have bound to which immunoglobulin molecules to establish a discriminatory image of antigen expression that is characteristic of a type of leukemia. Hoeffler merely teaches generally that the array methods disclosed therein may be used for diagnosing disorders. (*See also* Christopherson Declaration).

Terstappen fails to teach concurrent analysis of each immunoglobulin/antigen binding interaction and instead teaches a *sequential* analysis of *antibody pairings*. The document teaches that according to the method described therein, the sequence of the cell aliquot analysis and antibody pairing is important (*see* Terstappen, column 2, lines 51-65). Furthermore, modifying the method disclosed in Hoeffler according to the teachings of sequential analysis of antibody pairings in

Terstappen would change the principle of operation of Hoeffler, which is to analyze binding of more than one antibody to its respective antigen simultaneously. Thus, a person having ordinary skill in the art would not have found it obvious to combine the teachings of Hoeffler and Terstappen to obtain Applicants' claimed method that comprises establishing individual antibody/cell surface antigen binding interactions to provide a discriminatory image of antigen expression that is characteristic of a type of leukemia (*see, e.g., In re Ratti,* 270 F.2d 810, 813 (CCPA 1959) (holding that a *prima facie* case for obviousness had not been established when the suggested combination of references would require a reconstruction and redesign of the elements shown in the primary reference as well as a change in the basic principle under which the primary reference was designed to operate); MPEP § 2143.01).

Furthermore, Hoeffler fails to suggest, teach, or motivate a person having ordinary skill in the art to combine its teachings with any other prior art teaching to obtain the claimed method for identifying a type of leukemia. Terstappen also fails to provide any teaching, suggestion, or motivation to combine or modify the teachings of the prior art to produce Applicants' claimed method (*see also* Christopherson Declaration). Terstappen teaches a method for classifying leukemias that uses different techniques and analyses and does not remotely suggest any desirability to combine the teachings therein with any other prior art to achieve Applicants' invention. Even if each and every limitation of the present claims was found in the combination of cited documents, the PTO may not defeat patentability of the claimed invention by piecing together elements of the invention that may be found in the prior art without showing reasons why a skilled artisan would select those elements for combination in the manner claimed (*see In re Rouffet*, 149 F.3d at 1357). Applicants therefore submit that the Action has failed to establish a *prima facie* case of obviousness because the cited documents lack the requisite suggestion or motivation.

Accordingly, Applicants respectfully submit that all claims in the application satisfy the requirements for nonobviousness under 35 U.S.C. § 103 and request that these rejections be withdrawn.

Applicants respectfully submit that all claims in the application are allowable. Favorable consideration and a Notice of Allowance are earnestly solicited. In the event that the Examiner believes a teleconference will facilitate prosecution of this case, the Examiner is invited to telephone the undersigned at 206-622-4900.

Respectfully submitted,

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Enclosures:
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Petition for Extension of Time
Declaration under 37 C.F.R. § 1.132

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